

A few strong instincts and a few plain rules suffice us.

Ralph Waldo Emerson (1803–1882)

OBESITY

Childhood BMI Rises with Prenatal Exposure to Hexachlorobenzene

A prospective study published in the October 2008 issue of *Acta Paediatrica* has found an association between prenatal exposure to hexachlorobenzene (HCB) and being overweight or obese in childhood. The study was the first prospective look at prenatal exposure of HCB in a general population, says corresponding author Agnes Smink, now a research coordinator at consultancy SHL Group–Breda. The study relied on body mass index (BMI), a common gauge of overweight and obesity.

HCB is one of many organochlorine compounds restricted or banned by the Stockholm Convention on Persistent Organic Pollutants, which was signed in 2001. The compound was widely used,

starting in 1933, to kill fungi on crop seeds and in some manufacturing processes. Its commercial use in the United States ceased in 1965. HCB bioaccumulates in fat and breaks down slowly.

In humans, prenatal exposure to HCB has been shown to affect age at menarche and menopause, asthma, and fertility, as well as increase the relative risk of attention deficit/hyperactivity disorder. Other organochlorine compounds, including DDT and the polychlorinated biphenyls (PCBs), have also been implicated in causing damage *in utero*.

In 1997, the research group began recruiting expectant mothers on the Spanish Mediterranean island of Minorca. They measured HCBs, PCBs, the pesticide DDT, and the DDT metabolite DDE in umbilical cord blood of 405 children. The children's height and weight was measured at birth and at age 6.5 years.

Analysis showed that each doubling in cord blood HCB levels was associated with a weight increase of 1.14 kg (2.5 lb), but the children's height did not differ significantly. The relative risk of being overweight was a statistically significant 1.7 times higher per doubling in cord blood HCB level, and the relative risk for obesity was a nonsignificant 2.0 times higher. The association between HCB concentration and elevated BMI was independent of maternal socioeconomic status, weight, or education, or child's birth order or birth weight. There was no observed correlation between elevated BMI and PCBs, DDT, or DDE.

"This study provides an important piece of evidence that obesity may be related not only to junk food and lack of exercise but also to halogenated compounds or

endocrine disruptors," says Wilfried Karmaus, a professor of epidemiology at the University of South Carolina. In his study of Michigan women who ate large quantities of home-caught fish, maternal levels of DDE did correlate with BMI and weight in the women's adult children aged 20 to 50. That study, which relied on historic analyses of blood samples in which HCB had not been measured, will be published in a forthcoming issue of *Occupational and Environmental Medicine*.

The fact that different studies find different correlations between organochlorines and childhood obesity is troubling, Karmaus admits. "It bothers me a little bit that the Spanish found [a link with] HCB and we found [one with] DDE," he says. "But they are both endocrine disruptors, and they may work on a comparable mechanism. There is some indication that these substances may disrupt normal development or the metabolism of fat, but we don't know which substance and which mechanism."

Smink cautions that the new study does not suggest that HCB, or indeed any other organochlorine, is the sole explanation for overweight and obesity, which are estimated by the World Health Organization to affect at least 1 billion and 300 million people, respectively, worldwide. "It is important to keep in mind that a lot of factors are involved in the obesity epidemic," she says. "I think that the proportion of the ongoing obesity epidemic is minimal when it comes to HCB exposure. However, it is important to reduce prenatal exposure to toxicants like HCB to prevent health problems like overweight. It is not clear if the observed effects on body weight remain after the age of six years."

Because most HCB exposure comes through diet, especially meat, "a mother can prevent exposure by paying attention to where the local pollution sources are located and avoid eating food which has been grown there," Smink says.

"Pregnancy is a really important time for development," says Karmaus. "During pregnancy, you are exposed to [all the toxicants] your mother has collected in twenty or thirty years." Prevention is key, he says, because "as a fetus you can't decide not to live under these conditions." —David J. Tenenbaum



Child obesity may begin with prenatal exposures.

Michael Krinkel/stockphoto

MOLECULAR BIOLOGY

Telomerase Tells on Lifestyle

Being overweight, stressed, and sedentary have all been shown to accelerate the shortening of telomeres, DNA-protein complexes at the end of chromosomes that protect the genetic material and promote chromosomal stability. A new pilot study now finds that certain lifestyle changes may promote telomere integrity and length by significantly boosting telomerase activity in human immune cells.

Chromosomal stability is strongly correlated with longevity. Thus, if telomere length decreases prematurely, so also does life span. Shortened telomeres have been associated with a heightened disease risk (e.g., a 100-fold higher incidence of vascular dementia) and increased mortality rates for cancer and heart disease. Moreover, evidence published in the March–April 2006 issue of *Urologic Oncology* indicates that by initiating chromosomal instability, short dysfunctional telomeres may participate in prostate carcinogenesis. The leading hypothesis is that telomere attrition is influenced by oxidative stress (which can result from excessive body weight and stress as well as exposure to radiation and certain pollutants, such as airborne particles) and by inflammation (which generates and is perpetuated by oxidative stress).

Telomerase, an enzyme that directs the replication of telomeres, adds telomeric repeat sequences to the chromosomal DNA ends, explains principal investigator Elizabeth Blackburn, a molecular biologist at the University of California, San Francisco. “This preserves not only telomere length, but in the case of cells of the immune system, also healthy cell function and long-term immune function.” Nevertheless, she adds, “We do not yet know whether increasing telomerase activity could help reverse the problem of age-related telomere shortening.”

The study, reported online 15 September 2008 ahead of print in *Lancet Oncology*, assessed whether lifestyle changes could increase telomerase activity in peripheral blood mononuclear cells (PBMCs), an infection-fighting component of the immune system. The authors hypothesized that improvements in nutrition, exercise, and stress management—lifestyle factors thought to help prevent cancer and cardiovascular disease—might also bolster telomerase function.

Thirty men with biopsy-diagnosed, low-risk prostate cancer attended a three-day retreat followed by an outpatient phase. The men were asked to make comprehensive lifestyle changes: 1) adhere to a low-fat, primarily vegetarian diet supplemented with soy protein, fish oil, selenium, and vitamins C and E; 2) engage in moderate aerobic activity 30 minutes per day, 6 days a week; 3) practice stress management techniques such as yoga stretching, breathing, and meditation 6 days a week; and 4) attend a 1-hour support group once a week. Adherence was assessed by questionnaire. Changes in telomerase activity were measured at baseline and after 3 months.

Among 24 patients with sufficient PBMCs for longitudinal analysis, two-thirds showed a significant (29–84%) increase in telomerase activity, an indication of telomere restoration. This increase was also associated with significant decreases in low-density lipoprotein cholesterol and in one measure of psychological distress (intrusive thoughts). There were no significant changes in total levels of prostate-specific antigen, the marker for prostate cancer, nor was there evidence of cancer progression in the group.

“It seems remarkable that decreased stress and improved diet might give rise to measurable increases in telomerase activity in such a short time period,” says University of Glasgow biologist Pat Monaghan, who with Mark Haussmann coauthored a report on lifestyle and telomere dynamics in the January 2006 issue of *Trends in Ecology & Evolution*. Robert Sapolsky, a neuroendocrinologist at Stanford University, adds that the study “shows that [an] undesirable telomerase profile can be reversed with the sorts of lifestyle interventions that decrease the risk of various stress-related diseases.”

The potential confounding factors and limitations of the study—the small size and short duration of the study, the complexity of the lifestyle changes, the



Diet, stress, and exercise are important factors in chromosomal health.

absence of any data on the effect on telomere length, and the lack of an independent control group—make it impossible to identify causal factors. “Since these lifestyle changes and biological factors all tend to interact and reinforce each other, it’s difficult to determine which matter most,” says coauthor Elissa Epel, an associate professor of psychiatry at the University of California, San Francisco. Moreover, says Monaghan, the study involved a broad age range of men, and it is unknown whether the effects varied with the age of the patient.

Nevertheless, says Epel, the findings point to some provocative possibilities. “If we can improve our health behaviors, we might be able to reverse telomere shortening or at least stabilize the telomeres in our blood,” she says. Parsing out the most critical parts of the intervention is an important direction for future research. For now, Epel says, the take-home message is that what’s good for promoting cardiovascular health also seems to help curb cellular aging. This knowledge, in turn, could help motivate people to change their diet, exercise, and stress management habits for the better.

—M. Nathaniel Mead

CHILDREN'S HEALTH

Soil in the City: A Prime Source of Lead

Leaded gas was phased out in 1986, lead-based house paint a decade earlier. As a result, the percentage of U.S. children aged 5 years and younger exceeding the 10- $\mu\text{g}/\text{dL}$ blood lead level of concern established by the Centers for Disease Control and Prevention has dropped dramatically. On a national average, the rate fell from over 80% in 1976 to just below 2% in 2002. In many cities, however, it still commonly exceeds 15%. Why? A review published in the August 2008 issue of *Applied Geochemistry* points to urban soil as a lingering source of lead poisoning in children.

Review coauthor Gabriel Filippelli, chair of the Earth Sciences Department at Indiana University–Purdue University, Indianapolis, believes elevated blood lead levels in inner-city children come largely from exposure to lead dust that has settled over decades, resulting in soil whose lead content, at the most contaminated spots, can reach 100 times the background level of about 50 ppm. Children are typically exposed to this lead through play and hand-to-mouth activity.

In research published in the 15 December 2007 *Science of the Total Environment* (which was not included in the review article), Tulane University research professor and environmental toxicologist Howard W. Mielke and colleagues revealed a curvilinear relationship between soil lead in New Orleans and children's blood lead. The rate of increase was around 3 $\mu\text{g}/\text{dL}$ for every 1,000 ppm soil lead above 250–400 ppm, but the rate of increase of blood lead was 4 times higher at soil lead concentrations below 100 ppm. High lead levels damage children's nervous systems, stunt growth, delay development, and contribute to later-life delinquent behavior.

Filippelli mapped soil lead levels near Indianapolis roadways, tracking changes from older inner-city areas toward the newer suburbs. "In places such as the newer neighborhoods, far away from the urban core, where roads weren't so heavily traveled before leaded

gas was eliminated, you have noticeably lower lead levels," he says. "And when we overlaid a 1990s study of lead poisoning in children to the map we had developed, the distribution of cases fit our pattern precisely." This study, published with review coauthor Mark A.S. Laidlaw in the June 2005 issue of *EHP*, also showed that inner-city children had higher blood lead levels in the drier late summer months and lower levels in the winter. "We developed a meteorological prediction model that not only fit the results of our study over ninety percent of the time, but also showed a high degree of correlation with other cities as well," says Filippelli.

The review also looked at options for remediation of lead-contaminated urban soil. Removal of lead-contaminated soils and replacement with clean topsoil can cost more than \$1 million per acre, says Filippelli, who proposes two alternatives. "The simplest and least expensive would be a program of high-power shower-spraying of clean water during the months when soil conditions are at their driest, to keep lead-tainted soils from blowing onto horizontal surfaces and into homes." A second approach would be to put in a layer of clean soil and then hydroseed with grass. Filippelli plans additional experiments in Indianapolis next summer to gain a better picture of the cost and effectiveness of these and other options.

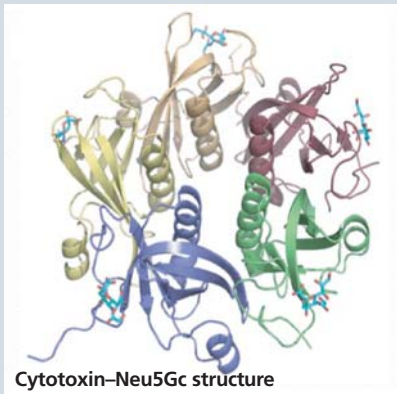
"I suspect that Filippelli's second proposal will be more effective and longer-lasting and—given the water supply issues of many cities—probably more attractive," says Mielke. In a study reported 15 April 2006 in *Environmental Science & Technology*, Mielke and colleagues reported success in covering heavily contaminated soils in New Orleans with low-lead alluvium from the Mississippi River.

The cost of remediation is certainly a factor, but the cost of inaction is also high. "Aggregate public health costs from lead poisoning in New Orleans alone run more than \$70 million annually," says Mielke, who points to proactive steps being undertaken in Norway. "The Norwegian government has begun testing and remediating soils at day care centers, elementary schools, and parks in major cities, while we dance around issues of responsibility and cost, spending millions in health care costs after using our children as bioindicators." —Lance Frazer

The Beat by Erin E. Dooley

Entré for Toxic Entrées?

When you eat red meat or cow's milk, you also consume *N*-glycolylneuraminic acid (Neu5Gc), a sugar molecule found in those foods, researchers reported 5 years ago. New work by the same group, published online



Cytotoxin-Neu5Gc structure

29 October 2008 ahead of print in *Nature*, shows moreover that subtilase cytotoxin secreted by Shiga toxigenic *E. coli*—also found in red meat and cow's milk—preferentially targets human cells carrying the Neu5Gc molecule. Humans were once presumed resistant to subtilase cytotoxin because they do not produce Neu5Gc. The new findings suggest, however, that eating contaminated meat can both expose people to foodborne illness and make them more vulnerable to it.

Little Fish Add Up

A study in the 2008 edition of the *Annual Review of Environment and Resources* finds that "forage fish" such as anchovies and sardines make up 37% of all fish harvested each year and that 90% of this highly nutritious catch is used in animal feed. Forage fish are an inexpensive alternative to the plant-based foods sometimes used in animal feed. The study authors state that the use of these fish for animal feed competes with human consumption of them in some developing countries, where they provide a crucial source

of protein and other beneficial nutrients. Overfishing of forage fish also harms populations of sea life that feed on them, such as cod, flounder, salmon, and tuna.

New Measures for Worker Health

In November 2008, the American College of Occupational and Environmental Medicine and the Integrated Benefits Institute sponsored a national summit to promote health and productivity management (HPM), a practice in which employers measure the health of their employees and their productivity levels in order to determine health-related costs and the effects poor health can have on productivity. These measurements can guide the design of prevention and health programs specific to the needs of a given industry. A consensus statement from the meeting will be forthcoming.

Island Nation's Insurance Policy

The Intergovernment Panel on Climate Changes estimated in 2007 the global average sea level could rise as much as 2 feet by 2100.

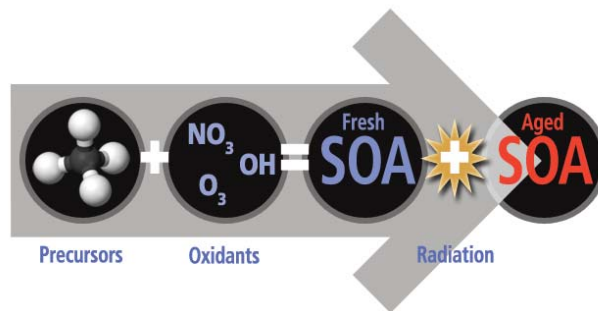
PARTICULATE MATTER

New Chapter on the Next Generation of Aerosols

Scientists have known for decades that carbonaceous molecules emitted by cars, factories, and ships can react chemically to form new pollutants called secondary organic aerosols (SOA). Until recently they thought these offspring constituted only a small part of the pollution plume [see “Ship Sulfate an Unexpected Heavy-weight,” *EHP* 116:A475 (2008)]. So when researcher Jose-Luis Jimenez of the University of Colorado at Boulder and colleagues analyzed the particle content of the air of Riverside, California, about 50 miles east of Los Angeles, they were surprised to find that only 10–30% came from smokestacks and tailpipes—the rest was SOA generated in the atmosphere. The findings, reported 15 October 2008 in *Environmental Science & Technology*, add to growing suspicions that people may be exposed to substantial levels of unregulated health-threatening pollutants.

Organic aerosols are formed from burning coal, gasoline, and other fossil fuels. Emissions of some primary organic aerosols are regulated by the Environmental Protection Agency (EPA). SOA forms when hydrocarbons (including toluene and xylene from fuel combustion) and other lesser volatile precursors oxidize and condense onto particles in the atmosphere. SOA also forms from terpenes and sesquiterpenes emitted by vegetation. Because SOA forms more readily in sunlight, it is more prevalent during the summer and in warmer climates. SOA disperses over wide areas, often far downwind of the cities where its precursors were emitted.

Particles contribute to preterm birth, low birth weight, asthma, and cardiovascular disease, among other health effects. Researchers think SOA may also threaten human health, but they're just starting to gather evidence to back that hypothesis. “We know a lot about what particles do, but we don't know a lot about the role of SOA in that,” says environmental epidemiologist Joel Schwartz of the



Harvard University School of Public Health. However, one clue lies in the size of SOA. “Smaller particles are more aggressive in finding their way into the lungs and crossing the blood barrier,” says atmospheric researcher Rainer Volkamer of the University of Colorado at Boulder. With a diameter of less than 1 μm , SOA is among the smaller particles in an ambient distribution.

A study in the October 2003 issue of *Inhalation Toxicology* showed a decrease in respiratory frequency in rodents exposed to ozone- and terpene-based SOA. First author Annette Rohr, senior technical manager of the Electric Power Research Institute in Palo Alto, California, says, “We had evidence of airway irritation as well as airflow limitation. There's no reason to think humans wouldn't have the same effect.” She notes, however, that the concentrations used in her studies were many times higher than likely human exposures.

EPA-funded studies under way in Los Angeles, Fresno, Pittsburgh, St. Louis, Boulder, Mexico City, and Chebogue Point (Canada) are looking at how emissions, temperature, wind, and other factors influence SOA formation and movement. Dan Costa, national program director for air research at the EPA, hopes that information eventually can be used to predict air quality. “We're trying to get fundamental information we can plug into models to project the air quality in a community,” he says. “But we're a ways away from being able to regulate these things.” —Cynthia Washam

Joseph Tarr/EHP

One of the islands of the Maldives



President-elect Mohamed Nasheed of the Maldives has taken that warning to heart. On 10 November 2008 he announced plans to create a “sovereign wealth fund” from tourism revenue to purchase land for relocation in the event the Maldivian homeland succumbs to rising sea levels. In an April 2008 book on the threat posed to his country by global warming, outgoing president Maumoon Abdul Gayoom wrote that the alternative to relocation—building protective walls around the 193 inhabited islands—was prohibitively expensive.

Pregnancy Hypertension Risks Higher for Rural Women

There are several well-known risk factors for preeclampsia, in which pregnant women experience high blood pressure and proteinuria. At the November 2008 annual meeting of the American Society of Nephrology, researchers announced one more. In a study of 362,000 women, they found that living in a rural county carried a 56% increased risk. This increase in risk, which the researchers believe may be linked to maternal poverty or social isolation, was independent of other risk factors including poor prenatal care.

Open Invitation to Oysters

Oysters purify water as they filter it through their bodies to obtain nutrition, with a single adult oyster filtering up to 60 gallons per day. Before the growth of the commercial shellfish industry in the last century, oyster beds along the Atlantic coast sometimes covered several square miles. Now oyster populations have been ravaged by overharvesting, pollution, and dredging. Environmental advocacy groups and

government entities have teamed up to create an artificial reef in Wellfleet Harbor, Cape Cod, in an effort to improve water quality, strengthen the local marine ecosystem, and form a natural breakwater to protect the shoreline. The reef is composed of two 100-foot lengths of “cultch,” or crushed shells, banked by mesh bags loaded with shells. In a second phase of the project, concrete structures will be added to serve as habitat for juvenile oysters. As of November 2008, hundreds of oysters had begun populating the reef.



Left to right: Craig Grobler, istockphoto